THE REACTIONS OF POLYMETHYLENE DERIVATIVES IN THE PREPARATION OF HIGHER OLEFINE PRIMARY ALCOHOLS.

DISSERTATION

Submitted in partial fulfillment of the requirements for the Degree of
Doctor of Philosophy in the Faculty of Pure Science
of Columbia University

By

EDWARD MARK SLOCUM, B.A. in Chem.

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TO MY FATHER AND MOTHER

ACKNOWLEDGMENT

I wish to acknowledge my indebtedness to Prof. Marston T. Bogert for his help and advice in this research, and to the Dupont De Nemours Co. for their financial aid. Also to the Rev. Winthrop Peabody for generous help in proof reading and correction.

Abstract of Dissertation

A general method has been developed for the preparation of the higher olefine primary alcohols. The reactions of halohydrin derivatives with sodium acetoacetic ester have been studied and a method developed whereby the ketols acetobutanol and acetopropanol can be prepared in 62% yield, a yield over twice than that given by previous methods.

It has been shown that the chlorhydrin derivatives appear to react with sodium acetoacetic ester almost exclusively in the enol form. It is suggested that this is a general result of the condensation of chlor derivatives with sodium acetoacetic ester.

The reaction of polymethylene dihalides with magnesium at low temperatures in the presence of aldehydes has been studied, and ethylene dibromide is shown to react normally at low temperatures. A method for the preparation of the disecondary glycol decandiol 4,7 has been worked out.

The reaction between halohydrin esters with magnesium in the presence of aldehydes and ketones has been studied under a number of conditions. The reactions of the methylene ethers of halohydrins with magnesium have been studied.

New Compounds Synthesized

Addition-Product of Hydriodic Acid and Trimethylene Glycol, M.P. c. 12°
Bromopropyl acetate
Symmetrical methylene ether of trimethylene iodohydrin
Methyl-(5)-heptandiol-(1,5)
Methyl-(5)-hepten-(5)-ol-(1)
Dimethyl-(4,6)-heptdien-(3,5)-ol-(1)
Methyl-(5)-nonen-(5)-ol-(1)
Dimethyl-(5,7)-octen-5-ol-(1)
Dimethyl-(4,7)-octen-4-ol-(1)
Decandiol-(4,7)
Nonyllactone

Improved or new methods for the following compounds:

Chlorpropyl acetate	Improved Method
Bromopropyl acetate	New "
Iodopropyl acetate	New "
Trimethylene bromhydrin	Improved "
Trimethylene iodohydrin	New "
Trimethylene dibromide	Improved "
Trimethylene diiodide	Improved "
Acetopropanol	New "
Acetobutanol	New "
Isobutyl alcohol	Improved "
Higher alkyl halides	Improved "
Disecondary glycols	New "

Use of sulphur bromide in preparing aliphatic bromides.
Higher substituted butyrolactones Improved Method

Historical Review

Ever since Schorlemmer in 1863 (5) demonstrated that the compound dimethyl was identical with ethane, one of the greatest potentialities in organic chemistry has been the synthesis of higher compounds of carbon by the linking up of carbon chains. By this means, many of the known acids, alcohols, aldehydes have been duplicated by laboratory synthesis and innumerable new compounds prepared.

In the open-chain or aliphatic compounds of carbon, an interesting class of compounds are the higher olefine primary alcohols. The three rose alcohols, geraniol, nerol and citronellol, are either mono- or diene primary alcohols. Other important perfume alcohols, such as farnesol in the aliphatic field and cinnamyl alcohol in the arylalkene series, are primary olefine carbinols. (114).

But very few higher primary olefine alcohols have been prepared synthetically. Of the hundreds of possible octenyl, nonenyl and decenyl primary alcohols, only one in each group is recorded in the last edition of Beilstein, as synthetically prepared. (13) (77) (90).

This research, therefore, has had for its purpose the working out of a method or methods whereby the higher primary olefine alcohols might be prepared in reasonable yield.

The halohydrin derivatives manifestly offer a promising means of introducing the $-CH_2CH_2OH$ and $-CH_2CH_2CH_2OH$ groupings into organic compounds. In 1896 (46) W. H. Perkin, Jr., attempted to condense glycol chlorhydrin with sodium malonic ester and with sodium acetoacetic ester, with no satisfactory results. Later (36) he tried phenoxyethylbromide in the place of the chlorhydrin, with better results but found the yields were still poor and the reactions complicated (46). Hamonet (Bul. (3), **33**, 515) (1905) also had poor yields with attempts to prepare butandiol ethers by a Fittig reaction on this halohydrin ether.

Later Hamonet (Bul. (3), **33**, 535-536) worked with the iodohydrin ether phenoxypropyl iodide, and found that by its means good yields of hexylene glycol could be obtained. Hamonet (71) used the amyloxyalkyl iodides and found they gave normal Grignard reagents with Mg in dry ether. With bromomethyl amyl ether Hamonet (105) found that the C(n+1) ether could be obtained from a given Cn alkyl magnesium halide.

Sommelet (102) showed that chlormethyl ether reacted with mercurized magnesium and the magnesien (Grignard reagent) so obtained gave with ketones mono-alkyl ethers of glycols. These mono ethers upon distillation with anhydrous formic or oxalic acid produced higher aldehydes. This reaction was efficient with ketones, or esters but produced poor results with aldehydes (102).

Gabriel (25) (27) (30) showed that potassium phthalimide reacts with an equivalent of ethylene dibromide to give phthalimidethyl

bromide. This compound by treatment with sulphuric acid at 200° C. is hydrolyzed to aminoethanol.

Butlerow (6), (7), studied the reactions of ethylene iodohydrin with zinc methyl and zinc ethyl. He obtained secondary alcohols, propanol-(2) and butanol-(2), instead of the primary alcohols to be expected.

Marvel and Tanenbaum (121) have recently used phenoxypropyl bromide in the synthesis of 1,4 dibrombutane.

In 1885 Lipp (21) prepared the ketols acetobutanol and acetopropanol, in 20% yields by condensing ethylene dibromide and trimethylene dibromide with sodium acetoacetic ester and hydrolyzing the condensation product. The ketol had a very wide boiling range. In 1889 W. H. Perkin (28) investigated this same condensation and showed that the substance which Lipp thought was the ketol was in reality its cyclic anhydrid.

In 1907 Franke and Kohn and Kovacevíc (78) increased the yield of the Lipp preparation 5% by adding the dibromide very slowly, drop by drop. They prepared two glycols from these ketols by the action upon them of methyl magnesium iodide. One of these glycols distilled unchanged when distilled at ordinary pressure (80), the other lost water and was converted into an olefine alcohol, (79). Franke and Kohn did not pursue the preparation any further (79).

Other investigators have likewise used the halohydrins in the preparation of carbinols or their derivatives. Fittig and Chanlaroff (26) condensed glycol chlorhydrin with sodium acetoacetic ester. By hydrolyzing the condensation product with barium hydroxide they obtained hydroxybutyric acid and butyrolactone. But Perkin was not able to reproduce these results (46) (36). Zelinsky and Moser (127) prepared the iodide of acetobutanol. This with magnesium gave the carbinol, oxymethyl-cyclohexane. F. Haller and Marsh (64) condensed bromethyl acetate with sodium acetoacetic ester. They made no attempt to hydrolyze the substituted acetoacetic ester. So it is not known whether their preparation was a keto—or enol—condensation product, or whether it would have been possible to obtain a ketol from it.

Sommelet (86) showed that the alkoxyketones in the Grignard reaction give mono-alkyl ethers of higher glycols. But he did not attempt to prepare either the ether or the free olefine alcohol from these glycol monoethers. Alberti (77) prepared among other products a nonenyl primary alcohol by the action of potassium hydroxide on the corresponding nonane chlorhydrin.

Noyes (41) showed that the dialkyl ether of hexylene glycol could be prepared by a Fittig reaction upon the methyl ethers of trimethylene chlorhydrin and of trimethylene iododydrin. (42)

Gauthier (97) prepared the dialkyl ether of an acetylene glycol by the action of chlor methyl methyl ether on the symmetrical magnesien of acetylene.

Dionneau (89) condensed chlormethyl ether with the magnesien of 1,5 dibrom-propane and obtained the dimenthyl ether of heptandiol (1,7) in 47% yield.

Grignard, Bodroux, Ahrens, Bischoff and Zelinsky (48) (57) (68) (75) (84) studied the reactions of the polymethylene dihalides with magnesium under various conditions. Their results will be discussed later.

Simonsen and Story (91) showed that chlormethyl methyl ether condenses with sodium malonic ester to give the expected methoxy derivative in small yield. Later (95) they found that sodium acetoacetic ester with chlormethyl ether condensed in the enol form.

V. Grignard (87) reported a method for the preparation of phenylethyl alcohol by the addition of ethylene chlorhydrin to two equivalents of phenyl magnesium bromide. The ether is distilled off and the residue heated on an oil bath. A vigorous reaction suddenly sets in and the magma swells greatly, with considerable evolution of heat. Upon decomposing the product with water, the saturated alcohol is obtained. Manifestly this reaction is suitable only for preparations on a small scale. In the aliphatic field and with the alkyl halides and halohydrins commonly available, the highest alcohol that could be prepared would be an octyl alcohol.

Methods of Preparation Investigated

Five methods that were thought to be possibilities for the preparation of higher olefine alcohols were as follows:

I. The reaction of magnesio-oxy-alkyl halides with aldehydes and ketones.

II. The reaction of halohydrin esters with magnesium or zinc in the presence of an aldehyde or ketone.

III. The reaction at low temperatures between polymethylene dihalides and magnesium in the presence of higher aldehydes and ketones.

IV. The reaction of methylene ethers of halohydrins with magnesium and aldehydes and ketones. The methylene ethers are decomposed by boiling with dilute acids into the free carbinol and formaldehyde.

V. The preparation of a ketol by the reaction between a halohydrin and sodium acetoacetic ester, and the reaction of this ketol with a suitable Grignard reagent. The elimination of the tertiary hydroxyl to form an unsaturated alcohol.

FLOW SHEET

(a) $F\,[CH_2]_n\,X + M \rightarrow F\,[CH_2]_n\,MX + RCOR' \rightarrow$

$$R-\underset{\displaystyle OMgX}{\overset{\displaystyle R'}{\underset{|}{\overset{|}{C}}}}\,[CH_2]_n\,F + H_2O \rightarrow R-\underset{\displaystyle OH}{\overset{\displaystyle R'}{\underset{|}{\overset{|}{C}}}}\,[CH_2]_n\,OH - H_2O \rightarrow$$

$$R-\overset{\displaystyle R'}{\overset{|}{C}} : CH\;[CH_2]_{n-1}OH$$

(b) $X\,[CH_2]\,X + 2M \rightarrow XM\,[CH_2]_n\,MX + 2RCOH \rightarrow$

$$R\,\underset{\displaystyle OMX}{\underset{|}{CH}}\,[CH_2]_n\,\underset{\displaystyle OMX}{\underset{|}{CHR}} + H_2O \rightarrow RCH(OH)\,[CH_2]_n\,CH(OH)R$$

(c) $F\,[CH_2]_n\,X + Na\,\underset{\displaystyle OCOCH_3}{\overset{\displaystyle COCH_3}{\underset{|}{\overset{|}{CH}}}} \rightarrow F\,[CH_2]_n\,\underset{\displaystyle OCOCH_3}{\overset{\displaystyle COCH_3}{\underset{|}{\overset{|}{CH}}}} + H_2O \rightarrow$

$$CH_3CO\,[CH_2]_n\,OH + 2RMgX \rightarrow R\,\underset{\displaystyle OMgX}{\overset{\displaystyle CH_3}{\underset{|}{\overset{|}{C}}}}\,[CH_2]_n\,OMgX + H_2O \rightarrow$$

$$R\,\underset{\displaystyle OH}{\overset{\displaystyle CH_3}{\underset{|}{\overset{|}{C}}}}\,[CH_2]_nOH\text{-}H_2O \rightarrow R\,C\,(CH_3) : CH\,[CH_2]_{n-1}OH$$

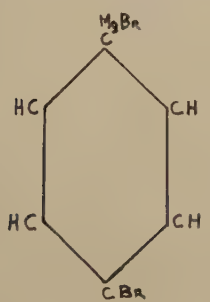
(d) $F[CH_2]_nX + Na\,CR(COCH_3)(OCOCH_3) \rightarrow F[CH_2]_n \cdot CR(COCH_3)(OCOCH_3) + H_2O \rightarrow$

$HO[CH_2]_n C(R)COOH - H_2O \rightarrow CH_2[CH_2]_{n-1}C(R)CO$ (O bridging)

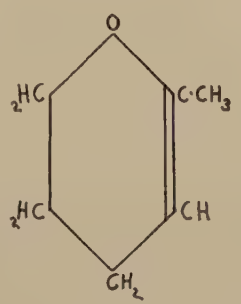
Where F = OMgI, —OCOCH$_3$, —OCH$_2$OCH$_3$, Br.
X = Cl Br or I.
M = Mg or Zn.
n = 2 or 3.
R′ = —H or —CH$_3$.
R = lower aliphatic radicle.

FORMULAS OF COMPOUNDS MENTIONED

IX. $2CH_2(OR)(OR') \rightarrow CH_2(OR)_2 + CH_2(OR')_2$
X. $C_6H_5CH(OMgBr)CH_2CH_2Br \cdot Et_2O$
XI. $HOOC[CH_2]_6COOH$
XII. $BrMgCH_2CH_2CH_2CH_2MgBr$
XIII. $BrMg[CH_2]_6MgBr$
XIV. $BrMgCH_2CH_2MgBr$
XV. $CH_2 : (OCH_2 \cdot CH_2 \cdot I)_2$
XVI. $CH_2 : (OCH_3)_2$
XVII. $CH_3 \cdot OCH_2 \cdot OCH_2 \cdot CH_2 \cdot CH_2 \cdot I$
XVIII. $BrMgC : CMgBr$
XIX. $Br \cdot Mg \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot Mg \cdot Br$
XX. $P + 3\,I \rightleftarrows PI_3$
XXI. $Br \cdot CH_2 \cdot CH_2 \cdot MgBr$
XXII. $CH_3OCH_2 \cdot O \cdot CH_2CH_2\,Cl$
XXIII.



XXIV.



Discussion of Results Obtained

As will be seen in the work following, it was found to be possible to condense iodohydrin derivatives with sodium acetoacetic ester and from the oxyalkylacetoacetic ester so prepared obtain ketols in good yield. These ketols with Grignard reagents gave the expected tertiary-primary glycols. These glycols when distilled at moderately reduced pressure lost water and formed the desired olefine alcohols.

But when chlorhydrin derivatives and (to some extent also bromhydrin) derivatives were used, the acetoacetic ester appeared to react almost exclusively in the enol form. Two other instances have been noted where chlor derivatives were found to produce an enol type condensation: Claisen (34) with chlorcarbonic ester and Simonsen and Story (95) with chlormethyl methyl ethers. In both of these former instances the halide is attached to a carbon to which oxygen is also attached. Such reagents might be regarded therefore as abnormal in themselves. Bouveault (55) noted that acid chlorides, where halogen and oxygen are united to the same carbon atom, gave a mixture of enol and keto condensations with sodium acetoacetic ester in alcohol solution. In a number of cases in the literature where chlor-products are reported to have given keto condensations, (29) (45) (124) it was found upon examination that no attempt was made by actual hydrolyses to ascertain definitely the constitution of the condensation product, or that very poor yields of keto-condensation product are reported (44) (124) (161). Ruhemann (37) (38) found that condensation with chlorfumaric esters apparently gave a furane derivative. But in the three chlorhydrin derivatives used in this research no such abnormal condition is present. In chlorethyl acetate, the chlorine and oxygen are bound to adjacent carbon atoms. In chlorpropyl acetate, the two groups are separated by a methylene group. Yet with ethylene chlorhydrin, chlorethyl acetate and chlorpropyl acetate, the reaction is almost exclusively in the enol form. It is to be noted also that the condensation with chlor derivatives was quite rapid, some 8 to 10 hours, whereas with iodo derivatives, it took some 30 to 50 hours of boiling to bring the reaction to completion. Brühl (72) has shown that sodium acetoacetic ester is apparently mainly in the enolic form. In alcoholic solutions it is probable that the two isomers exist side by side, with the enol form in large excess. Hence a chlor compound which can react with the enol derivative gives a speedy condensation. But the iodo compound which reacts mainly with the keto sodium derivative takes a very much longer time to complete its reaction.

In the investigation of the reaction of polymethylene dihalides with magnesium at low temperatures, the dihalides were found to react normally as (XIV), not abnormally or asymmetrically as Ahrens, Bischoff and Zelinsky found. Other disubstituted magnesiens, such as

(XVIII) and (XIX), are found to react as simple symmetrical derivatives, not as an asymmetrical or dimeric derivative.

Kohler (111) found the olefine ketones to react abnormally with Grignard reagents at ordinary temperatures. But Kyriakides (104) showed that below 0° these same olefine ketones reacted normally with Grignard reagents. This would be in line with the normal results found in this work at low temperatures.

The haloalkyl esters are found to react with magnesium under proper conditions precisely as when the halogen is substituted in the acid radicle: Tingle (107) and Röttinger (99).

The reaction is generally brought to a standstill, as in so many reactions between metals and organic compounds, by the formation of an adhesive layer of condensation product on the surface of this metal, thus preventing completion of the reaction (99). Whenever the product of the reaction is soluble in ether or other solvent, the method is a useful one for the preparations desired.

In the action of the three halide acids on trimethylene glycol, quite marked differences are observed. Hydriodic acid and hydrobromic acid (47) both form solid crystalline addition products with this glycol which on heating rearrange almost quantitatively into the halohydrin and water. Hydrochloric acid not only forms no observable stable addition product with this glycol, but its action on the glycol at 150° C. is exceedingly slow.

When the glycol is treated with an acetyl halide, like differences are observed. With acetyl bromide a 20% yield of unesterified brompropyl alcohol is obtained along with the brompropyl acetate, but no trimethylene glycol monoacetate is found.

With acetyl chloride the yield of chlorpropyl acetate is small and of trimethylene glycol monoacetate quite large (80%).

When the glycol is treated with a mixture of acetic acid and hydriodic acid, iodopropyl alcohol and iodopropyl acetate are formed but no observable amount of glycol monoacetate.

With this glycol, acetyl bromide apparently acts as a bromiding agent, primarily, not as an acetylating agent. In the reaction of an alcohol with an acetyl halide there is no fundamental reason why an acetic product should result any more than an alkyl halide (VII).

With acetyl chloride the more usual formation of an acetate is the prominent result. But with acetyl bromide, the formation of a bromide appears to be the predominant result with these glycols.

In the usual explanation of the esterification of alcohols by mixtures of acetic and hydrochloric acids, we generally ascribe simply a catalytic action to the hydrochloric acid on the alcohol-ester equilibrium.

But if hydriodic acid be used, a notable proportion of alkyl iodide will result, as well as the alkyl acetate. With trimethylene glycol the tendency to form the iodo compound is much stronger than to form the acetate.

It would seem, therefore, that our usual explanation as to the mechanism of esterification in the presence of strong acids is incomplete for it applies only to those strong acids which do not form very stable addition products with the usual alcohols. In such cases, the ester probably forms a stable addition product (Kendall) (120). But when the alcohol itself forms a stable addition product with the mineral acid used, the alkyl halide will form a noticeable and even a predominant proportion of the reaction product.

The crystalline addition product of trimethylene glycol and hydriodic acid, for instance, may be taken as an oxonium substitution product of hypoiodous acid.

Just as hypoiodous acid upon heating breaks down into iodine and water (Friend) (106), so this compound when distilled gives water and the iodohydrin.

A method has been worked out for the preparation of higher lactones containing a primary carbinol group, by the condensation of an iodohydrin derivative with the sodium salt of a substituted acetoacetic ester, and the hydrolysis of the condensation product. By this method nonyllactone has been prepared with a yield of 50%. Fittig-Chanlaroff (26) in 1887 prepared butyrolactone by condensing sodium acetoacetic ester with ethylene chlorhydrin. He does not state his yield, and on repetition of his work the amount of lactone obtained was very small. Perkin also, as mentioned before, states (46) (36) that he could not duplicate Chanlaroff's results. With iodo derivatives yields of 50% can be obtained.

Preparation of Intermediates

A. ALKYL IODIDES.

In the preparation of the alkyl iodides the method of Adams and Vorhees (115) was modified so as to obviate the use of his special apparatus with the higher alcohols (C_3 to C_5) and still allow the use of yellow phosphorus with its advantages of better yields, cleaner product, etc.

The alcohol (3 moles) and red phosphorus (1 atom) are mixed and cooled with running water. 3 atom-weights of iodine are weighed into a bottle; about 50 grams of this iodine are placed in a second flask and some of the alcohol is poured onto the iodine to dissolve it. While dissolving, this mixture is cooled with tap water so as to prevent rise of temperature. When the iodine is all dissolved the solution is poured onto the red phosphorus in the main reaction flask, keeping this flask cool with running water. A second lot of iodine, a little larger than the first is dissolved as before, and poured into the main reaction flask. So on until all the iodine has been added to the reaction flask. It is then kept cool for an hour or so and allowed to stand over night in the distillation apparatus.

The next morning, the receiving flask is filled half full of finely cracked ice and the delivery tube of the condenser brought well to the bottom of the receiving flask. Ten to twenty grams of yellow phosphorus are added to the reaction mixture. The flask containing the reaction mixture is heated very gently until slight bubbles are seen to rise to the surface. The reaction is then allowed to initiate itself quietly. Most times the reaction begins very easily and satisfactorily, but every now and then the reaction begins very violently. Even in such cases the cracked ice is able to prevent any great loss of alkyl halide. The yields are generally over 90%.

The theory behind this process is as follows: Adams and Voorhees noticed that some yellow phosphorus was always left unattacked in spite of the greater reactivity of yellow phosphorus over red phosphorus. They made no explanation of this fact but merely noted it. (117). Now it is probable that the speeds of reaction between the iodine and the two varieties of phosphorus are a function of the surface exposed to reaction of the two substances. The red phosphorus being a powder has a much greater surface. The greater part of the iodine has already reacted with the red phosphorus so that, since there is an excess of phosphorus, some of both isomers remain.

The value of the yellow phosphorus appears to be that its equilibrium (XX) lies much farther to the right than is the case with the red phosphorus in these alcohol systems. If this be true, there is no need of adding the yellow phosphorus until just before heating begins.

The greater part of the iodine has already reacted with the red phosphorus so that only a small amount of yellow phosphorus is needed to combine with the iodine left untouched by the red phosphorus. And the results given by the above preparations substantiate this reasoning. The alkyl halide obtained is only tinged a slight yellow and there is no formation of phosphonium iodide or foaming at the end of the distillation. Neither is there any danger of explosion upon opening the empty reaction flask. Care should be taken in disposing of the flask residue as yellow phosphorus is still present.

In the preparation of isobutyl alcohol, it was found that ordinary commercial isobutyl alcohol consists largely of normal propyl alcohol. Several fractionations with a ten bulb fractionating column did not help materially in separating these alcohols, as constant boiling mixtures with water are present. It was found, however, that a convenient rough separation could be made by extracting the mixture with water. Propyl alcohol is soluble in water in all proportions, but isobutyl alcohol is soluble only to the extent of ten per cent. Three extractions with water left an isobutyl alcohol which gave an 80% yield of isobutyl iodide, B.P. 119-122°. (B.P. 120° (137)).

Prep. No.	B.P.	Alkyl Iodide.	Preparation.	Yield.
1	102 ° (133)	N.propyl Iodide	102°-103°	90%
2	89.6° (134)	Isopropyl Iodide	88°- 89°	92%
3	129.9° (136)	N.butyl Iodide	128°-129°	94%
4	120 ° (137)	Isobutyl Iodide	119°-122°	80%
5	147 ° (138)	Isoamyl Iodide	145°-148°	85%

B. ALKENE DIHALIDES:

6. **Ethylene dibromide:** B.P. 131.6° (130); 129° (131). Commercial ethylene dibromide was distilled twice and fraction taken 130-131°.

7. **Trimethylene dibromide:** B.P. 165° (132). Three moles of trimethylene glycol were treated with a slight excess over two moles of PBr_3. The references in the literature (2) (116) indicate that phosphorus pentahalides have been used in the past when the dihalides have been made from a glycol by the use of a phosphorus compound. But it was found in this work that the liquid tribromide does just as well as the solid pentabromide. Yield 85% of theory, of dibromide boiling 164°-168°.

8. **Trimethylene diiodide:** B.P. (Not without decomposition) 227° (135). This halide can be prepared by a similar method to the dibromide. The yield is poorer, about 60% (B.P. 210-220) (with decomposition) and would probably be improved by the use of an excess of iodine. This preparation was merely a tentative one, and convenient apparatus for distillation under reduced pressure was not available. For this reason, the distillation was made at ordinary pressure.

C. GLYCOL ESTER.

9. **Trimethylene monoacetate:** B.P. 202.5° (129). Trimethylene glycol was cooled and an equimolar quantity of acetyl chloride added with shaking. The mixture was then distilled at once and the product fractionated to separate the chlorhydrin acetate (B.P. 166°) from the trimethylene glycol monoacetate (B.P. 202°). 50% yield of mono ester boiling at 200-203°.

Saponification Value: 1 gram required .489 grms of KOH.
Calculated for $C_5H_{10}O_3$: .474 grms of KOH.

PREPARATION OF HALOHYDRINS AND THEIR DERIVATIVES: The following halohydrins and their derivatives were prepared for this work:

D. ETHENE DERIVATIVES:

10. **Ethylene chlorhydrin:** B.P. 132° (139) Commercially available chlorhydrin was fractionated several times in vacuo until upon redistillation at atmospheric pressure it had boiling point 131°-133°.

11. **Chlorethyl acetate:** B.P. 145° (157). Twice the theoretical amount of acetyl chloride was added slowly to ethylene chlorhydrin well cooled with ice. The mixture was allowed to stand over night and then heated on the water bath under return condenser till no more HCl is evolved. The excess acetyl chloride was then distilled off and the product neutralized and dried with $CaCl_2$. It was then distilled; B.P. 144-147°. Yield 90%.

A similar method was used by Direck and Bissel (110) in the preparation of chlorpropyl acetate from trimethylene chlorhydrin.

Henry (9) observed that acetyl choride converted ethylene chlorhydrin into its acetate, but he did not note the necessity for a large excess of acetyl chloride to acetylate completely the hydroxyl group.

12. **Methoxy-methyl ether of ethylene chlorhydrin** (XXII). Dry HCl gas was passed into a mixture of 1 mole methyl alcohol, 1 mole trioxy-methylene (as HCHO) and 1 mole ethylene chlorhydrin. The trioxy-methylene dissolved and water separated out. The product was dried and distilled under reduced pressure (25 mm.) It seemed to distill badly and high boiling polymers were found. The use of the undistilled crude reaction product, after drying with calcium chloride, was therefore attempted.

Würtz (Ann. Chim. Phys. (3), **48**, 373) prepared methyl-ethyl acetal by heating acetaldehyde, ethyl and methyl alcohols with sulphuric acid. Pratesi (20) prepared methylene ethers by treating a mixture of trioxymethylene and alcohols with a mineral acid and distilling. Henry (54) observed that the methylene ethers of the chlorhydrins are not at all stable. For instance, the treatment of symmetrical chlorethyl ether of methylene glycol with a methyl alcohol solution of sodium iodide breaks it down into the dimethyl ether of methylene glycol (methylal) and free ethylene iodohydrin.

13. **The (symmetrical) methylene ether of ethylene chlorhydrin.** B.P. 218° at 760 mm. (34). The method of Henry (34) was followed Dry HCl gas was passed into a mixture of molar ethylene chlorhydrin asd trioxymethylene until the solution was saturated with HCl. A second mole of ethylene chlorhydrin was added and mixture heated on water bath and then distilled in vacuo. B.P. 115°-120° at 22mm. Yield 55%.

Ethylene bromhydrin. Preparation of ethylene bromhydrin or its derivatives was not attempted.

14. **Ethylene iodohydrin.** B.P. (not without decomposition) 176° at 760 mm. (31). The method of Butlerow (6) was followed. An excess of potassium iodide was dissolved in methyl alcohol and ethylene chlorhydrin added. The mixture was then heated on the water bath. Iodine rapidly separated and a precipate of potassium chloride formed. The conversion of the chlorhydrin to iodohydrin was not complete and product had to be fractionated. The yield of iodohydrin boiling at 175-178° was small, not over 20%. Distillation at ordinary pressure was carried out because at the time there was no opportunity for distillation under diminished pressure, and the preparation was merely a tentative one.

15. **Iodoethyl acetate.** B.P. 110° at 60 mm. (126). Chlorethyl acetate was added to an excess of potassium iodide dissolved in methyl alcohol. The reaction was much cleaner than with ethylene chlorhydrin and not so much free iodine formed. The reaction also was much more complete. The iodoethyl acetate boiled at 108-112° at 60 mm. Yield 70% of the theoretical. The preparation of iodoethyl acetate in this manner has not been recorded in the literature, but Henry (40) used a similar method to prepare iodopropyl acetate.

E. TRIMETHYLENE DERIVATIVES:

16. **Trimethylene chlorhydrin:** B.P. 160-164° (110). For the preparation of trimethylene derivatives trimethylene glycol, as obtained in crude form from the Globe Soap Co. was used. This was distilled twice in vacuo, until it boiled at 125-127° at 25 mm. Two methods of preparing trimethylene chlorhydrin were tried: (A) By the action of S_2Cl_2 on trimethylene glycol.

Derick and Bissell (110) prepared trimethylene chlorhydrin by the action of sulphur chloride on trimethylene glycol with a 60% yield. This method is unpleasant to work, as a precipitate of sulphur containing occluded sulphur chloride and trimethylene chlorhydrin comes down, which is a nuisance. Due to losses from the sulphur mass, the yield obtained was 50% instead of 60% of preparation boiling 160°-164°. (B). As suggested by Ladenburg, (19) dry HCl gas was passed for 8 hours into trimethylene glycol heated on the water bath. The yield was very poor, not more than 10%. Ladenburg (19) found that after 16 hours treatment at 148° only 60% of glycol was converted to its chlorhydrin. Trimethylene glycol reacts with HCl no faster than ethylene glycol.

16a. **Chlorpropyl acetate:** B.P. 162°-166°, (110) (This work 165-166°) The following methods were used to prepare this ester:

(A) Addition of acetyl chloride to cold trimethylene glycol and heating on water bath. This preparation of chlorpropyl acetate is not mentioned in the literature, but Lourenco used a similar method, (4), for the preparation of chlorethyl acetate from ethylene glycol.

(B) Addition of acetyl chloride to cold trimethylene glycol in presence of dry sodium carbonate. This method apparently had not been tried before.

(C) Addition of acetyl chloride to trimethylene chlorhydrin as previously prepared, after the method of Derick and Bissel. (110).

(D) Addition of acetyl chloride to trimethylene glycol and heating the mixture in closed soda water bottles for 8 hours on the water bath. This preparation for chlorpropyl acetate has not been recorded in the literature but Lourenco (4) used a somewhat similar method in the preparation of chlorethyl acetate.

(E) Addition of acetyl chloride to trimethylene glycol in which zinc chloride has been dissolved and heating the mixture in closed soda water bottles for 8 hours on the water bath. This modification has not apparently been tried before.

(F) Action of PCl_3 on trimethylene glycol monoacetate and $ZnCl_2$. This method has not been tried before.

(A) This method gave only about 15% of the chlorhydrin acetate, and 50% of trimethylene glycol monoacetate, (B.P. 202°) with a probable 20% additional monoacetate in the higher middle fraction.

(B) This method gave 30% of the chlorhydrin and 65% of crude monoacetate.

(C) This method, as outlined by Derick and Bissell (110), gave about 90% yield from the chlorhydrin or 54% yield on the original glycol. The acetyl chloride must be in large excess and the heating on the water bath continued for some time after all the HCl has seemingly come over.

(D) This method gave 70% yield of the chlorpropyl acetate from the original glycol. The low yield of the former methods (A) and (B) was due obviously to the easy escape of the HCl formed; the use of a soda water bottle held this HCl in contact with the reaction mixture and so facilitated the formation of the chlorpropyl ester.

(E) The addition of $ZnCl_2$ further favored the production of the chlorhydrin ester, so that yield of 80% was obtained. This is probably the best method available for the preparation of chlorpropyl acetate.

(F) Dehn and Davis (85) obtained excellent yields of alkyl chlorides from the action of PCl_3 on alcohols in the presence of fused $ZnCl_2$. This was tried with trimethylene glycol monoacetate but the yields were not satisfactory, mostly water soluble phospho-compounds being formed.

17. **Trimethylene bromhydrin**: B.P. 98°-112° at 185 mm. (18); this work, (80°-82° at 22 mm.) This was prepared by two methods: (A) By action of S_2Br_2 on trimethylene glycol. (B) By action of HBr on the glycol.

(A) Sulphur bromide was made by adding two atomic weights of sulphur to two atomic weights of bromine. The mixture grew warm and changed in color. The typical odor of the sulphur halides was noticed. This compound was then added to an equivalent quantity of trimethylene glycol. The mixture warmed at once and sulphur was precipitated; as in the sulphur chloride method for the chlorhydrin, the precipitated sulphur lessens the yield by occluding halohydrin which is hard to recover. The yield was about 60%. B.P. 80-82° at 22 mm.

This reaction of sulphur bromide on a glycol had not previously been recorded. In fact, sulphur bromide is used very rarely in organic preparations. The only reference found was in Abderhalden IV, 942 to A. Edinger and P. Goldberg (52) where sulphur bromide had been used to brominate aromatic hydrocarbons.

(B) Dry HBr gas was made by the method of Derick and Hess (113). Sand, red phosphorus and water are mixed in a flask and bromine dropped in slowly. The gas is washed with red phosphorus in concentrated hydrobromic acid and dried by phosphorus pentoxide. It is passed into the trimethylene glycol, kept cold by ice and salt. Toward the end of the reaction trouble is caused by the blocking of the HBr tube by the formation of the solid addition product of HBr and trimethylene glycol (M.P. 52°) (47). The mixture is allowed to stand over night and heated on the water bath and distilled in vacuo. The yield of product (B.P. 80-82° at 22 mm.) is better than with the sulphur bromide method, 74% on the HBr used.

Frühling (18) prepared this bromhydrin by passing into a mixture of the glycol and fuming hydrobromic acid a current of HBr, without cooling the reaction mixture. The yield and purity of the product is much improved by keeping the reaction temperature low and excluding water, as far as possible.

18. **Brompropyl acetate**: B.P. 88°-90° at 22 mm. (This work) was prepared in two ways:

(A) By the action of acetyl chloride on the bromhydrin (Derick and Bissel's Method) and (B) by the action of acetyl bromide on trimethylene glycol. This is apparently a new method.

(A) This acetylization was the same as with the chlorhydrins. As before the acetyl chloride must be in large excess and the mixture heated for some time after evolution of HCl has ceased. The yield of ester B.P. 88°-90° at 22 mm. is over 90% of theory.

(B) Phosphorus tribromide was prepared by adding bromine to red phosphorus. A small amount of bromine was added at first; the phosphorus caught fire and burned until all the oxygen in the flask was consumed; the addition of the bromine could then go on in an atmosphere of nitrogen. The reddish phosphorus tribromide was digested with excess of red phosphorus over night. The next morning it was quite clear. It was poured off and added to glacial acetic acid and well mixed. Two layers formed. The mixture was then distilled slowly into an equivalent quantity of trimethylene glycol kept cold by ice and salt. The reaction mixture was allowed to stand over night and heated on the water bath for an hour. It was distilled in vacuo (25 mm). At first acid water comes over and then the brompropyl acetate.

The brompropyl acetate as thus distilled is contaminated with the bromhydrin. Acetyl chloride is added and the mixture heated for several hours under reflux. It is neutralized, dried with $CaCl_2$ and distilled. The first fraction is tested with acetyl chloride as the bromhydrin accumulates in the first fraction. If this fraction heats up upon adding to it acetyl chloride, the whole product must be acetylized a second time with acetyl chloride to esterify thoroughly the bromhydrin. The yield is quite good, 85%. The brompropyl acetate boils at 88-90° at 22 mm. Brompropyl acetate had not been hitherto prepared, nor has acetyl bromide been used previously in preparing bromhydrin esters. Analysis: Calculated for $C_5H_9O_2Br$: Br, 44.4%. Found: Br, 44.8%.

19. **Trimethylene iodohydrin**: B.P. 225° at 760 mm (40). This was prepared by two methods:

(A) By the addition of HI to trimethylene glycol cooled by ice and salt. (B) The addition of HI to trimethylene glycol diluted with benzene.

(A) Dry hydriodic acid was made by the method given in Roscoe and Sch. Vol. I, 208. It was dried by P_2O_5 and passed into trimethylene glycol cooled with ice and salt until half an equivalent weight of HI had been absorbed. The HI is very quickly absorbed, the mixture grew thick due to the formation of a solid addition compound of hydriodic acid and trimethylene glycol, hitherto unobserved. Finally the mixture grew too solid to stir, so an equal quantity of dry ether was added to dilute and soften the mixture and the addition of an equivalent weight of hydriodic acid completed.

The magma was allowed to stand over night and then heated on the water bath to draw off the ether. A slight odor of ethyl iodide could be noticed and the mixture was very dark from separated iodine. The oil was distilled under reduced pressure (25 mm) giving water and crude iodohydrin. The latter was redistilled under reduced pressure (25 mm). The yield of iodohydrin after distilling was 68%. This method of preparing trimethylene iodohydrin is not mentioned in the literature. B.P. 110-113° at 15 mm.

(B) Trimethylene glycol was mixed with an equal volume of benzene. It was chilled with ice and salt and dry HI gas passed into it as before. The yield of iodohydrin was 92%, with same properties as preceding preparation. These preparations of trimethylene iodohydrin have not been recorded in the literature, but Simpson (3) prepared ethylene iodohydrin by passing HI gas into ethylene glycol. Ethylene glycol forms no addition compound with hydriodic acid, so that this preparation is simple and needs no special precautions to bring the reaction to completion.

20. **Iodopropyl acetate**: B.P. 207-210° at 757 mm; 112-115° at 38 mm. (40). This had been prepared by Henry from chlorpropyl acetate by treatment with NaI solution. Its preparation for this research was tried by treating an equimolar mixture of trimethylene glycol and glacial acetic acid with dry HI gas. After this method had been worked out it was found that a similar method had been described by Simpson in an early volume of the Annalen (3) for the preparation of iodoethyl acetate from ethylene glycol.

A molar mixture of trimethylene glycol and glacial acetic acid is chilled below O° C by an ice-salt mixture. Dry HI gas is then passed in until the weight of the flask shows that an equivalent amount of HI has been absorbed by the mixture. The flask is allowed to stand over night, heated on the water bath for one hour, and distilled under vacuum (25 mm), into a well-cooled receiving flask. Acid water comes over first and then the iodopropyl acetate.

As with bromopropyl acetate, the ester contains a notable proportion of free iodohydrin, so that the oil must be heated on the water bath with acetyl chloride until the first fraction shows no rise in temperature when mixed with acetyl chloride. The yield of iodopropyl acetate boiling 98-100° at 15 mm. was 88% when some five pounds of the ester was prepared. Analysis: Calculated for $C_3H_5O_2I$;I, 55.7%. Found: I, 55.8%.

21. **Methoxy-methyl ether of trimethylene iodohydrin.** (XVII). Two methods of preparation were tried: (A) Treating a mixture of molar methyl alcohol, trimethylene iodohydrin and trioxymethylene with dry HCl gas until the trioxymethylene dissolves. (20):(B). Heating trimethylene iodohydrin was an excess of chlormethyl methyl ether (35).

(A) HCl gas was passed into a mixture of methyl alcohol, iodohydrin and trioxymethylene until the mixture was clear. The flask was heated on the water bath and then distilled. It was found to consist mainly of the symmetrical methylene ether of iodohydrin (XV) with methylal (XVI) and some (XVII). Fractional distillation seemed to rearrange the unsymmetrical ether into the symmetrical ethers, for the fraction boiling 130°-150° at 15 mm produced continually the symmetrical ether boiling at 185°-195° at 15 mm as well as the low boiling methylal. See (IX) on page (11).

This reaction is probably brought about by the high vapor pressure of the methylal, (XVI). As mentioned before, Henry found these methylene ethers of the halohydrins to be very unstable (54). Traces of the lower alcohols easily replace the higher alcohols in these methylene ethers (119). They are also readily hydrolysed by acids. Therefore, if a trace of acid remains in the material at the time of distillation, it will hydrolyse a small portion of the methylene ether. The methyl alcohol thus freed will replace the iodopropyl radicle with the formation of low boiling methylal. The removal of this upsets the equilibrium and the cycle is again gone through with. Delapine (49) has shown that equilibrium conditions obtain with these acetals. They all dissociate sufficiently to give odor of formaldehyde.

(B) Chlormethyl methyl ether B.P. 59° (143); 50°-60° (142) was prepared by the method given by Wedekind (142). A molar mixture of anhydrous methyl alcohol and trioxymethylene was saturated in the cold with dry HCl gas. The trioxymethylene dissolved and the liquid separated into two layers. It was found best not to separate the layers but to distill them both together.

The distillate from 40° to 70° is taken and dried well with $CaCl_2$. It is distilled again and the fraction 50-60° taken as chlormethyl methyl ether. It is not advisable to attempt to heat the ether any more than is absolutely necessary as it evolves HCl and condenses. To the excess of this chlormethyl ether, the iodohydrin is added. The mixture heats up and is heated for some time on the water bath under a reflux. It is allowed to stand over night and distilled under vacuum.

When an equivalent plus 50% excess of chlormethyl ether is mixed with trimethylene iodohydrin the mixture warms and HCl gas is given off. The mixture was warmed on the water bath and allowed to stand twelve hours. The excess chlormethyl ether was distilled off and the product fractionated in vacuo. Even at a vacuum of 11 mm the unsymmetrical ether rearranged into the symmetrical methylene ether of trimethylene iodohydrin and methylal. About 10 c.c. of a fraction boiling 160°-170° at 11 mm was obtained which is probably the unsymmetrical ether.

22. **(Symmetrical) methylene ether of trimethylene iodohydrin.** Twe methods were tried: (A) Passing HCl gas into a mixture of 1 mole trioxymethylene and 2 moles trimethylene iodohydrin until the trioxymethylene disappeared. (B) Saturating a mixture of molar quantities of trioxymethylene and trimethylene iodohydrin with HCl gas, and then adding a mole of iodohydrin.

The first method had been used by Stappers (70) to prepare the (symmetrical) methylene ether of propylene chlorhydrin. Henry (54) employed a similar method to that of (B) to prepare the (symmetrical) chlorethyl ether of methylene glycol.

(A) This method (70) appeared to give poor results. The reaction mixture grew very dark with separated iodine, and upon dis-

tillation at 14 mm. pressure, much free formaldehyde and iodohydrin came over. Yield of methylene ether, B.P. 188-192° at 15 mm, 35%.

(B) This method was the more satisfactory one. Upon distillation at 12 mm. a 60% yield of the symmetrical ether, B.P. 188-193° at 12 mm. was obtained.

This iodohydrin methylene ether is a thick yellowish oil with a slight odor of formaldehyde when heated. It is soluble in alcohol, ether and acetone and slightly soluble in water. Boiling with 20% sulphuric acid hydrolysed it to formaldehyde and iodopropyl alcohol.

PREPARATION OF HIGHER ALDEHYDES AND KETONES FOR REACTION WITH HALOHYDRIN DERIVATIVES

The following carbonyl compounds were prepared or purified for use in this research:

Aldehydes: Butaldehyde, heptaldehyde, benzaldehyde.

Ketones: Butyl methyl ketone, amyl methyl ketone, isoamyl methyl ketone, hexyl methyl ketone, isohexyl methyl ketone, methyl nonyl ketone, acetophenone.

Unsaturated ketones: Mesityl oxide, methyl heptenone.

The preparations were as follows:

F. ALDEHYDES:

23. **Butaldehyde:** B.P. 75° (144). Normal butyl alcohol was oxidized by sodium dichromate and sulphuric acid solution while boiling on the water bath. The distillate was boiled with dilute acid to hydrolyse the acetals and fractionated with a 10 bulb fractionating column. Yield of butaldehyde boiling at 74-76° was 28% of the theoretical.

24. **Heptaldehyde:** B.P. 154° (146) Castor oil was distilled at 100 mm. pressure and the distillate fractionated. The fraction 150-160° was treated with freshly made sodium bisulphite lye. The crystalline addition product was washed twice with benzene and then broken up with dilute acid. Product boiled 154-155°. Yield about 10%. References (1) (12) (15).

25. **Benzaldehyde:** B.P. 179° (159). Commercial chlorine-free benzaldehyde was dried with anhydrous sodium sulphate and distilled in vacuo. The fraction boiling at 67-68° at 15 mm. was taken as benzaldehyde.

G. KETONES:

26. **Butyl methyl ketone:** This, the amyl, isoamyl and the isohexyl methyl ketones were prepared by the condensation of normal propyl iodide, normal butyl iodide, isobutyl iodide, and isoamyl iodide on the sodium compound of aceto-acetic ester.

It was also attempted to use the corresponding alkyl bromides and to replace part of the expensive absolute alcohol with dry benzene. But the reaction became very slow, taking over one hundred hours' boiling, and the reaction products upon hydrolysis proved to be mainly a compound with the enol isomer of acetoacetic ester.

For large amounts of acetone were recovered and the yield of the higher ketone desired was very small. The influence of the solvent and the halide radicle is thus seen on the course of this condensation. This is discussed in connection with the condensation of halohydrins with sodium acetoacetic ester.

The following preparation as outlined by Latham Clarke (94) was used. The alkyl iodide was added to the absolute alcohol solution of sodium acetoascetic ester, and boiled under a reflux. In some 30 hours the reaction of the liquid became neutral. The alcohol was distilled off, and the sodium iodide washed out with water. The oil after distillation at 25 mm. was boiled under reflux with 5% KOH solution in H_2O for 2 hours and then distilled with steam. The oily distillate was fractionated with a fractionating column.

Prep.	B.P.	Ketone.	Preparation.	Yield.
26	B.P. 127° (145)	Butyl methyl ketone,	B.P. 125-128°	60%
27	B.P. 149°, 152° (147) (148)	Amyl methyl ketone,	B.P. 148-152°	65%
28	B.P. 144° (149)	Isoamyl methyl ketone,	B.P. 140-146°	62%
29	B.P. 162°, 166° (151) (152)	Isohexyl methyl ketone,	B.P. 160-165°	55%

30. **Hexyl methyl ketone:** B.P. 172° (150). This was prepared by the dry distillation of neutral, dry castor oil soap. The method outlined by Chapman (8) and Neison (10) was followed. The oil as obtained was fractionated and the fraction 160-180° was treated with freshly made bisulphite lye. The crystalline addition product was washed twice with benzene and decomposed by cold dilute acid. The ketone boiled 170-172°. Yield 5% on castor oil used.

31. **Nonyl methyl ketone:** B.P. 118° at 18 mm. (153). Oil of rue was shaken with strong freshly made bisulphite lye. The crystalline addition product was washed twice with benzene and decomposed by dilute cold acid. The ketone boiled sharply at 125° at 25 mm. Yield 80% of oil.

32. **Mesityl oxide:** B.P. 129.5-130° (154). Commercial diacetone alcohol was heated with a trace of free iodine, as suggested by H. Hibbert (108). The yield of mesityl oxide, B.P. 128-131°, was quite good, about 70%.

33. **Methyl heptenone:** B.P. 84° at 56 mm. (155) probably misprint for 36 mm. The method published by Verley (43) was followed. 500 grams of citral was boiled for 12 hours with five liters of a 10% solution of potassium carbonate. The oil was then separated and distilled under vacuum. The first fraction boiling below 80° at 25 mm. was kept separate and the remaining oil again boiled 12 hours with this potassium carbonate solution. This dark oil is again fractionated in vacuo and the first fraction reserved. In this way it took nearly a week to break down half a liter of citral. The yield of methyl heptenone boiling 82-86° at 36 mm. was 36% of the theoretical.

34. Through the courtesy of the Standard Oil Co. of New Jersey, some 15 pounds of still residues from their distillations of petrohol (isopropyl alcohol) was fractionated for higher secondary alcohols. After a number of distillations fractions boiling within five degrees were obtained, but these all centered about the boiling point of the symmetrical carbinols. For instance, of the octanol fractions, the fraction centered about 71° at 10 mm., the boiling point for octanol(4), rather than 76°, the boiling point for octanol(2).

One hundred grams was therefore oxidized with acid chromate solution and treated with strong freshly made bisulphite lye. Only a slight amount dissolved and upon acidification just two or three drops of oil appeared. Thus the possibility of any great amount of methyl ketones from this source was negatived.

35. **Acetophenone.** B.P. 202° (160). The preparation of the Eastman Laboratories was dried with anhyd. sodium sulphate and distilled at 18 mm. B.P. 91°-92°.

METHODS USED.

I. THE REACTION OF HALOHYDRIN ESTERS WITH MAGNESIUM IN THE PRESENCE OF CARBONYL GROUP:

One mole of ethyl iodide was added slowly to two atoms of magnesium filings. When the reaction was complete, one mole of ethylene chlorhydrin was added. A grayish white precipitate came down. A mole of acetophenone was added and the mixture boiled under reflux condenser for 24 hours. But no attack of the magnesium was apparent.

The ether was then boiled off and residue heated on oil bath. An unsaturated gas was given off, but no reaction appeared with the magnesium. With ethylene iodohydrin similar results were obtained, except that iodine seemed to split out of the mixture very easily when heated on the oil bath.

II. THE REACTION OF HALOHYDRIN ESTERS WITH MAGNESIUM IN THE PRESENCE OF CARBONYL GROUP:

One atom of magnesium filings was placed in anhydrous ether and a little iodine added. An equimolar mixture of brompropyl acetate and the ketone or aldehyde used was added slowly at room temperatures. After a short time the magnesium would begin to be attacked. But generally the magnesium addition product was a heavy viscous oil which soon coated the magnesium and blocked the reaction. With chlorpropyl acetate it was very hard to start the reaction even. Mercurizing the surface of the magnesium, as suggested by Sommelet (102), had a little beneficial effect.

With iodopropyl acetate, the reaction started quite easily but the product was generally as insoluble and viscous as with brompropyl acetate.

With activated zinc-copper couple (118) no result was obtained. Treat Johnson (98) using amalgamated zinc in the Reformatski reaction encountered the same type of conditions and obtained only two percent yields.

The ketone mesityl oxide gave a magnesium addition product that was soluble in anhydrous ether. This upon hydrolysis and distillation gave a 60% yield of the alcohol, dimethyl4,6-heptdien3,6-ol (1).

Dimethyl4,6-heptdien3,6-ol(1): b.p. 78-80° at 18 mm. is a pale yellow oil with an intense sweet odor of cedar. It is soluble in the usual organic solvents and insoluble in water. It decolorizes a solution of bromine in carbon tetrachloride. It gives an ester with acetic anhydrid.

Analysis. Calculated for $C_9H_{16}O$: C,77.1%; H,11.3%.

Found: C, 77.4%; H, 10.9%.

Use of Magnesium Amalgam: As an amalgam is not wetted by viscous oils or ether solutions, it was thought that an amalgam of magnesium might obviate this blocking of the reaction by the formation of an adhesive insoluble layer on the reactive surface of the magnesium. Solid magnesium amalgam was prepared by Evans' method (60). This was rapidly dropped into anhydrous ether to prevent attack by moisture of the air.

The reaction of this magnesium amalgam on equimolar mixtures of brompropyl acetate and heptaldehyde was very violent. The main product of the reaction was a viscous resin. Reduction was apparently occurring because the distillable product of the reaction (about 5%; B.P. 70-82° at 25 mm.) was mainly normal heptyl alcohol (B.P. 175° (140)). There are a number of instances where Grignard reagents act as reducing agents (66) (67) (74) (90). Hence it was attempted to moderate and modify the course of the reaction by lowering the temperature, by diluting the reacting material, and by using an amalgam with smaller magnesium content. In no case was the amount of non-distillable resin appreciably reduced.

Results with butaldehyde, benzaldehyde, and methyl butyl ketone were similar in the formation as the main product of the reaction of a viscous nondistillable resin.

Finally it was noted that Kling and Roy (83) had discovered that aldehydes, etc., are violently attacked in dry ether solution by magnesium amalgam with the formation of 90% non-distillable resin and 10% of a glycol. This explained the formation of a high boiling resin. This is probably an aldehyde resin of high molecular weight and combines with what magnesium compound is formed. Water is probably liberated in the polymerization, as in the formation of croton-aldehyde from acetaldehyde. This attacks the magnesium amalgam and reduces part of the aldehyde present to the corresponding alcohol. No glycols were observed, as the dimeric aldehyde probably combines with the magnesium compound instead of reducing to a carbinol grouping. For the preparation of Grignard reagents, when carbonyl compounds are not present, magnesium amalgam works excellently. It is an excellent drying agent, due to the absence of any oxide film over the surface of the metal. Therefore it will remove traces of water from the ether, etc., used in the preparation.

Grignard Reaction at Higher Temperatures: The reaction of brompropyl acetate with saturated ketones and plain magnesium at higher temperatures was then tried. The saturated methyl alkyl ketones are considerably more stable bodies than are aliphatic aldehydes. Spencer and Crewdson (93) had shown that alkyl iodides react with magnesium without the presence of ether at elevated temperatures. Brompropyl acetate, or preferably iodopropyl acetate, two moles, mixed with one mole of methyl butyl ketone was added to one atom of magnesium filings, and the whole heated on an oil bath in an atmosphere of hydrogen. When the temperature reached 130-135° a

very vigorous reaction took place, with the formation of a solid magnesium compound. This swelled greatly and the reaction ceased with about one-third of the magnesium unattacked. This was due to the absorption of the excess halohydrin acetate by the solid magnesium compound, and the consequent exhaustion of reaction material near the magnesium filings.

The use of three or four moles of iodopropyl acetate did not help greatly, as the absorptive power of the spongy magnesium compound appears to be very great. No high boiling diluent could be found that did not interfere markedly with the initiation of the reaction.

Upon decomposing the magnesium compound with water, and fractionating the oil so obtained, it was found that a considerable portion of the magnesium compound had been broken up into low boiling olefine hydrocarbons. A yield of about 30% of the desired alcohol was apparently obtained but this was contaminated by the mother ketone. The odor of these higher ketones is a very intense amyl acetate-anise odor, so powerful as to mask completely the odor of the alcohol formed.

Amyl methyl ketone, isoamyl methyl ketone, and hexyl methyl ketone were all tried with the same result. Due to the absorption of the halohydrin acetate by the spongy magnesium compound, some of the ketone always remained unattacked. The powerful odor of the ketone almost completely masked the odor of the carbinol produced. The process, therefore, appeared unreliable for the production of olefine alcohols free from the odor of the parent substances.

III. THE REACTION AT LOW TEMPERATURES BETWEEN POLYMETHYLENE DIHALIDES AND MAGNESIUM IN THE PRESENCE OF ALDEHYDES AND KETONES.

Grignard and Tissier (48) found that ethylene dibromide at ordinary temperatures gave ethylene and magnesium bromide as the main products of their reaction. Bodroux (57) found that para-di-brombenzene gave with magnesium in ether an unsymmetrical magnesien (XXIV).

Ahrens (68) found that when the reaction between ethylene dibromide and magnesium is carried on at O° C., and benzaldehyde is added, a grayish precipitate forms which upon analysis gave figures agreeing with the theoretical percentages for the compound (X). But upon hydrolyzing this compound with water the main product is not the expected bromhydrin but benzaldehyde and ethylene. Bischoff (75) investigated this reaction in the presence of ketones and esters. Bischoff found that the reaction is greatly retarded if phenetole, ethyl acetate, benzil or benzene be added. It is prevented altogether when acetone, acetophenone, benzophenone, ethyl oxalate, ethyl malonate or ethyl succinate are present.

Zelinsky (84) found that when CO_2 is added to the reaction product of trimethylene dibromide and magnesium after heating the ether solution on the bath, a 25% yield of glutaric acid (XI) is obtained. This would tend to show that in such solutions a notable proportion of (XII) was present even after the ether solution had been boiled under reflux on the water bath.

It would seem, therefore, from the work of Ahrens and Zelinsky that some sort of a Grignard reagent is formed especially at low temperatures, although from Bischoff's work it would appear that a Barbier-Grignard reaction, where the magnesium is allowed to react upon a mixture of carbonyl compound and halide compound, would not take place. But if a Barbier-Grignard reaction could be brought about in the presence of an aliphatic ketone or aldehyde, it was possible that a bromhydrin might be formed. This by loss of water and saponification of the resulting bromide could be expected to give an olefine primary alcohol. All this is, of course, contingent upon an unsymmetrical product of the reaction between magnesium and the polymethylene dibromide in the Grignard reaction.

Upon adding slowly an equimolar mixture of ethylene dibromide and butaldehyde to magnesium in dry ether cooled to 0° C., a vigorous reaction took place with some evolution of an unsaturated gas (ethylene?). When the ether solution was allowed to warm up, evolution of gas increased markedly. But by keeping the flask well cooled by a salt-ice mixture, the evolution of gas could be kept down to a minimum. A heavy gray precipitate came down, which filled most of the flask. The reaction product was allowed to stand over night. The next morning the magma was poured upon ice and the ether solution separated and treated in the usual manner.

When distilled, some butaldehyde and ethylene dibromide was recovered. A fraction boiling between 100° and 125° at 15 mm. was probably the butaldol and its dehydration product from the action of anhydrous magnesium bromide on butaldehyde, or possibly a cyclic oxide.

The greater part of the oil distilled between 125° and 155° at 15 mm. This upon further fractionation gave a 40% yield of a somewhat viscous yellowish oil boiling 143-147° at 15 mm. This oil contained no bromine (109) and was lighter than water. It had a pleasant fruity odor and gave a vigorous reaction with acetic anhydrid. This acetate had a fruity odor. Neither decolorized a carbon tetrachloride solution of bromine.

Manifestly, the reaction of the ethylene dibromide with magnesium has been a symmetrical one and instead of a bromhydrin a glycol has been formed, decandiol(4,7).

Analysis. Calculated for $C_{10}H_{22}O_2$: C, 68.9%; H, 12.6%. Found: C, 68.4%; H, 12.28%.

Experiments with heptaldehyde and methyl isoamyl ketone, with trimethylene dibromide and Mg, showed vigorous reactions. With

heptaldehyde the reaction appeared more complex; beside the high boiling heptadecane glycol, above 200° (12 mm.) there appeared a lower fraction of boiling point around 125° at 12 mm. It is possibly a cyclic hydrocarbon, a rearrangement of the diolefine corresponding to the glycol.

It would appear from this work that Ahrens' statement that at low temperatures ethylene dibromide reacts with magnesium to give an unsymmetrical magnesien (XXI), has very little to substantiate it, even though this statement has been repeated in text books such as VonRichter. Zelinsky (84) found that the trimethylene dibromide compound with magnesium existed at the temperature of boiling ether mainly in its dimeric form (XIII). This present work would tend to show that at lower temperatures the system reacts in the simple form (XIV) as well as in the dimeric form. This is in line with the results found by Zelinsky, when working with the higher polymethylene dihalides.

The inference to be drawn from Bischoff's work, that the Barbier-Grignard reaction does not occur with the alkylene dihalides, is negatived for the higher aliphathic aldehydes and ketones. The reaction with the dihalides is more sensitive to moisture than the simpler reaction with the usual alkyl monohalides. Perhaps if Bischoff's work with acetophenone and benzophenone could be repeated with very pure ether and ketones, the reaction would be found to proceed normally.

IV. THE BARBIER-GRIGNARD REACTION WITH METHYLENE ETHERS OF THE HALOHYDRINS.

Chichibabin (103) has shown that methylene ethers are not attacked by Grignard reagents, hence the methylene ether of a halohydrin ought to form stable magnesiens.

The unsymmetrical methylene ethers being so unstable, it was found by experiment inadvisable to consider them as preparation material.

The symmetrical methylene ether of trimethylene iodohydrin was tried in a Barbier-Grignard reaction with isoamyl methyl ketone. Very little action could be noticed even after two days standing. The ether was boiled off and the residue heated on an oil bath. A vigorous reaction soon appeared and a viscous tough magnesium addition product resulted. This was insoluble in ether and slowly decomposed by water and acohol.

The main distillable product (145-155°) from its odor (resembling c. octyl alcohol) was probably methyl(5)hexanol(2) the secondary alcohol obtained by reducing isoamyl methyl ketone (B.P. 148-150°) (141). It is possible that the methylene ether dissociates sufficiently at high temperatures to give formaldehyde which with the magnesium acts as a reducing agent.

The methylene ethers were thus found to possess no advantage in the preparation of higher primary alcohols. The methyl methylene ethers of the halohydrins are too instable, and the symmetrical halohydrin ethers react very slowly with magnesium in dry ether, at ordinary temperatures and dissociate at high temperatures.

V. THE PREPARATION OF ACETOBUTANOL AND ITS EMPLOYMENT FOR THE SYNTHESIS OF HIGHER OLEFINE PRIMARY ALCOHOLS.

In this present work a new synthesis of the ketol acetobutanol has been worked out, giving a yield of over twice that obtained by the method (of Lipp) hitherto standard. This ketol has been used to synthesize C_8 to C_{10} primary olefine alcohols—a class of alcohols difficult of synthesis by other known methods. By this present method a higher primary olefine alcohol, such as C_{10} primary alcohol, can be prepared in only three operations, all with comparatively good yields and of convenient laboratory operation.

New method for preparation of acetobutanol: B.P. 225-227° (156). The old Lipp method gave very low yields of the desired ketol because 80% of the dibromide used went to form the symmetrical condensation product, diacetoxypimelic ester. It appeared, therefore, the most logical thing to do would be to replace the second bromide atom by a grouping which would not allow the formation of the substituted pimelic ester.

Chanlaroff (26) had prepared oxybutyric acid and butyrolactone by the condensation of glycol chlorhydrin and sodium acetoacetic ester and the saponification of the substituted ester with barium hydroxide.

The oil was then boiled for 8 hours with 5% hydrochloric acid. nearly always promotes the formation of ketone, it was expected that if the barium hydroxide saponification were replaced by a weak acid saponification the desired oxy-ketone, (or ketol) would be obtained.

Equimolar quantities of sodium acetoacetic ester and brompropyl acetate in absolute alcohol solution were boiled over a free flame until a slight amount of the alcohol solution when added to phenolphthalein in water proved to be neutral. The excess of absolute alcohol was then distilled off and the substituted acetoacetic ester extracted by ether. The ethyl ether and remaining alcohol were distilled off and the oil so obtained distilled in vacuo until the temperature of the distillation was above 100° at 15 mm. The heating was then stopped. It was not attempted to distill the whole of the condensation product, as Perkin had shown how easily a similar product condenses to form a tetrahydropyrone derivative (24). By this distillation all the unreacted acetoacetic ester, brompropyl acetate and traces of ethyl alcohol would be removed so that the substituted acetoacetic ester to be hydrolysed would not be contaminated with these parent substances.

The oil was then boiled for 8 hours with 5% hydrochloric acid. At first the evolution of carbon dioxide was very vigorous. It slowed down and for the last three hours no evolution of gas was remarked. The water solution was then saturated with potassium carbonate and extracted with ether. The ether was distilled off by careful distillation with a 10 bulb fractionating column. Most of the remaining material had a very low boiling point, only about 20% boiling above 100°.

Acetobutanol itself boils 226-227° (156) but it has two unfortunate characteristics. It has very stable hydrates and breaks down at 155-160° to form a low-boiling anhydrid B.P. 109° (28) (XXIII). To break up the hydrates the material was digested for several days with fused potassium carbonate. The greater portion still had a boiling point below 100°. This was taken to consist mainly of the impure anhydrid. To convert this into the high boiling open chain ketol, it was treated with water in small quantity. But no marked conversion could be observed. Perkin (27) states that the anhydrid absorbs water very quickly; that the mere standing with the requisite quantity of water for some days will convert the anhydrid quantitatively to the ketol. But a week's standing did not have this effect, nor did some twelve hours' refluxing under a return condenser. It was subsequently found that this material was mainly acetone.

It was decided to repeat the acetoacetic ester condensation using chlorhydrin derivatives instead of bromhydrin so as to check directly the work of Chanlaroff. W. H. Perkin, Jr. (36) (46) had been unable to repeat Chanlaroff's work with glycol chlorhydrin and methylacetoacetic ester. Even when preparing butyrolactone, Perkin found it advisable to use phenoxyethyl bromide in the place of chlorhydrin. Equimolar amounts of sodium acetoacetic ester and ethylene chlorhydrin were boiled under reflux condenser with free flame. The condensation was quite rapid. Eight to ten hours boiling completed the reaction. The substituted acetoacetic esters were extracted and purified as before. They were hydrolyzed with 5% hydrochloric acid, the solution sataurated with ignited potassium carbonate and extracted many times with ether. Upon careful distillation practically all the material distilled below 100° and the greater part between 55-60°. This was identified as acetone by the melting point of its benzaldehyde compound (110°). Saponification by baryta water gave a 3% yield of butyrolactone.

By the previous distillation in vacuo of the condensation product, all but traces of the unsubstituted acetoacetic ester had been removed. But it was evident that the greater part of the product of the hydrolysis of the substituted acetoacetic ester was acetone. The condensation product, it was obvious, must be mostly the product of sodium acetoacetic ester in its enol form. This upon weak hydrolysis would give acetone, ethyl alcohol and ethylene glycol as it products.

The halohydrin esters chlorethyl acetate and chlorpropyl acetate were next tried to ascertain if the reaction of sodium acetoacetic ester

in its enol form was brought about by the presence of the free hydroxyl group in the chlorhydrin. With both esters the result was the same; the main product of the hydrolysis was acetone.

The iodohydrin acetate was last of all tried. This gave an excellent yield of condensation product boiling above 100° at 25 mm. (88%). Upon hydrolysis and extraction, all of the product boiled above 70° at 25 mm. vacuum. The condensation of iodopropyl acetate with sodium acetoacetic ester was therefore with the acetoacetic ester in its keto form and not its enol form.

But in attempting to purify and fractionate the acetobutanol it was found that the ketol was extraordinarily sensitive to impurities. The oil would be distilling quietly until without warning water would begin to come over and the boiling point would drop to 60° or 70° at 25 mm. Attempts to prevent this anhydrid formation by digestion of the ketol with fused potassium carbonate appeared only to increase the trouble.

Finally it was found that the best procedure was to allow the anhydrid and water to distill over together, taking precautions by thorough cooling of the receiver to see that neither water nor anhydrid were lost. The turbid mixture was then heated on the water bath for a couple of hours, when the water disappeared and the viscous ketol was reformed. The process must be repeated until the impurities have been distilled out and the ketol will then distill without decomposition. A 62% yield of acetobutanol (B.P. 111-118° at 15 mm.) (B.P. 225-227°) (156) was in this way obtained, a yield over twice that of the best preparation hitherto. It is probable that the actual yield of ketol is practically quantitative but the difficulties of slow extracting with ether hindered the complete exhaustion of the water solution. A somewhat wide boiling range was taken, due to the bad bumping and easy superheating of the ketol in large quantity.

The Grignard Reaction: The following Grignard reagents were prepared, ethyl magnesium bromide, isopropyl magnesium iodide, isobutyl magnesium iodide, normal butyl magnesium iodide and iso amyl magnesium iodide. For one mole of the ketol 2½ moles of ethyl magnesium bromide were used, for the other four, 3½ moles. From the ethyl magnesium iodide, an 80% yield of the glycol was obtained (B.P. 140-145° at 12 mm.) The yields of the glycol fraction from the higher Grignard reagents were poorer, about 60%. This is probably due to the low content of actual alkyl magnesium halide present in these Grignard reagents.

Gilman (122) has recently shown that even in so simple a Grignard reagent as ethyl magnesium iodide only 88-90% is present as true alkyl magnesium halide. With isoamyl iodide, it appears that not more than 35% was present as a true "magnesien."

The Grignard reactions themselves were of the usual type. The ketol diluted with five volumes of anhydrous ether was dropped slowly into the cold Grignard reagent. Each drop caused the formation

of a grayish clot of magnesium compound. When all the ketol had been added, the solution was shaken thoroughly to allow full contact of the ether solution on the precipitate. The flask was allowed to stand over night. A gray magma then filled half the flask with a clear ether solution above it. The ether solution still contained a magnesium compound in solution.

The mass was poured onto cracked ice and and acidified with glacial acetic acid. The ether was removed and the water extracted three times with ether. The ether solution was neutralized with sodium carbonate solution and dried. The ether was removed and the oil so obtained distilled in vacuo. The first fraction, to 100° at 12 mm., was kept separate. With the four higher glycols, the glycols broke down to olefine alcohols upon distillation even at 12 mm.; no attempt, therefore, was made to isolate them.

Removal of water to form unsaturated alcohol: The glycols so obtained were distilled several times at 250 mm. pressure to split off water from the tertiary carbinol group. The water so split off could be seen distilling over with the oil. It seemed to be difficult to remove this tertiary hydroxyl group completely. Even after three distillations there would be a slight high boiling fraction which would lose water. At the same time a slight amount of diene olefines are produced by the splitting off of water from the primary alcohol group as well. So it is not worth while to repeat the distillation at 250 mm. pressure any more times than is necessary.

The crude olefine alcohols were then fractionated at 12 mm. vacuum. Finally fractions boiling within two degrees were obtained. The yields of these fractions were from 40 to 60 % on the weight of the crude glycol fraction. But the yield of actual olefine alcohol is really much higher, probably 80% on the glycol. The fraction contaminated with slight amount of glycol, and hence boiling slightly higher than the olefine alcohol, was generally as large as that of the alcohol fraction itself. In larger preparations it would be possible to fractionate this higher fraction more closely and so increase largely the yield of the main fraction.

Higher primary olefine alcohols prepared from acetobutanol.

Methyl(5)hepten(4)ol(1) or **Methyl(5)hepten(5)ol(1):** The tertiary-primary glycol, methyl(5)heptandiol(1,5) boils without apparent decomposition 140-145° under 12 mm. pressure. Even when heated with an excess of acetic anhydrid it does not lose water but forms a diacetate which distills at a temperature very slightly lower than the glycol itself. But the diacetate upon distillation at 250 mm. pressure breaks off acetic acid and forms the acetate of the olefine alcohol methyl5hepten50l-(1). The free acetic acid is removed by treatment with aqueous sodium carbonate and the ester saponified by alcoholic potassium hydroxide, the alcohol so obtained being identical with that derived by direct dehydration of the tertiary primary glycol.

Methyl5hepten5ol(1) is directly obtained by distilling at 250 mm. pressure the glycol methyl5heptandiol (1,5), the product of the action of ethyl magnesium bromide on acetobutanol. Water distills over with the oil and the oil upon drying has a boiling point some thirty degrees lower than that of the glycol. After fractionation in vacuo, a fraction is obtained boiling within two degrees, 92-94° at 15 mm. with 58% yield on weight of glycol.

This alcohol is a sweet-smelling oil, insoluble in water but soluble in the usual organic solvents.* It decolorizes a solution of bromine in carbon tetrachloride and forms an acetate with acetic anhydrid. It is resinified by concentrated sulphuric acid.

Analysis: Calculated for $C_8H_{16}O$; C, 75.0%: H, 12.5%. Found: C, 74.2%; H, 12.44%**.

The reaction products of isopropyl magnesium iodide and normal propyl magnesium iodide with acetobutanol.

The reaction between isopropyl magnesium iodide and acetobutanol appears to be more complex than that given by the other magnesiens used in this work. A high boiling product was obtained which was apparently the tertiary-primary glycol to be expected. This on distillation lost water as usual but seemingly produced a very complex mixture of compounds which proved difficult to fractionate. Finally a fraction boiling 106-108° at 15 mm. was separated with a yield of 32% of the theoretical on the weight of the crude glycol.

This oil gave all the usual reactions of an unsaturated alcohol, but upon combustion it gave precentages of carbon and hydrogen entirely too low for such a C_9 alcohol but agreeing quite well for the unsaturated alcohol from the dehydration of the glycol produced by the reduction of acetobutanol. This glycol is known and has a boiling point some thirty degrees above that of the oil obtained in this reaction. (Hexandiol 1, 5) B.P. 140-141° at 17 mm. Frobe, (53). The unsaturated alcohol hexen(5)ol(1) is not known but should have a boiling point around 140° at 760 mm. Whereas this preparation boiled 66° higher.

Carbon	Found	Calculated for $C_9H_{18}O$	Calculated for $C_6H_{12}O$
	72.1%	76.0%	72.0%
	71.9%		
	70.9%		
	Spoilt		
Hydrogen	11.74%	12.67%	12.0%
	11.90%		
	11.97%		
	12.05%		

*See note 1, p. 40.

*See note 3, p. 40.

It is also to be noted that the oil in question has an unpleasant, rank odor whereas the other alcohols made have quite pleasant odors.

A small run of normal propyl magnesium iodide with acetobutanol gave after the usual procedure an oil boiling 105-112° at 15 mm. with a very unpleasant, weedy odor. Nothing further was done with this preparation.

A number of cases have been noted where Grignard reagents have acted as reducing agents. (66) (67) (74) (90)

Methyl(5)nonen(5)ol(1)

The glycol methyl(5)nonandiol(1, 5) b.p. 145-155° at 14 mm, obtained from the action of normal butyl magnesium iodide on acetobutanol, loses water upon distillation even at a vacuum of 14mm.

Methyl(5)nonen(5)ol(1)* B.P. 109-111° at 11 mm. From the above glycol. Colorless oil with sweet aromatic odor. Soluble in all the usual organic solvents** but insoluble in water. It decolorizes a solution of bromine in carbon tetrachloride. With acetic anhydrid it forms an acetate.

Analysis. Calculated for $C_{10}H_{20}O$; C, 76.9%; H, 12.79%. Found: C, 75.9%; H, 12.57%.***

Dimethyl(5,7)octen(5)ol(1): The primary-tertiary glycol dimethyl(5, 7)octandiol(1, 5) from the action of isobutyl magnesium iodide on acetobutanol boils around 150° at 12 mm. pressure but breaks down and loses water even at this pressure.

Dimethyl(5,7)octen(5)ol(1)*. From the above glycol B. P. 103-108° at 12 mm. On account of an accident, this product could not be fractionated further. Colorless oil with heavy sweetish aromatic odor. Soluble in the usual organic solvents and insoluble in water. It decolorizes a solution of bromine in carbon tetrachloride. With acetic acid anhydrid it forms an acetate, of pleasant flowery odor.

Analysis. Calculated for $C_{10}H_{20}O$: C, 76.9%; H, 12.79%. Found: C, 75.9%; H, 12.57%***.

V (b) The reaction of acetopropanol with the higher magnesium reagents.

Preparation of acetopropanol: B. P. 207-208° (decomp). (78): An equimolar mixture of sodium acetoacetic ester and iodoethyl acetate is boiled for some twenty-six hours until the reaction to phenolphthalein is neutral. The excess of absolute alcohol is distilled off and the acetoxy-ethyl-acetoacetic ester freed from mother compounds as in the preparation of acetobutanol. The substituted acetoacetic ester is saponified by boiling with 5% hydrochloric acid for eight hours. The solution is saturated with ignited potassium carbonate and extracted repeatedly with ether. The ketol is purified as in the pre-

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*See note 2, p. 40.
**See note 1, p. 40.
***See note 3, p. 40.

paration of acetobutanol. The yield is lower, some 50%, and the preparation is more difficult to purify. Its boiling point is 100-106° at 15 mm. It does not bump as badly upon distillation in vacuo as acetobutanol.

The Grignard Reaction with acetopropanol: Three and a half moles of isoamyl iodide were added to 3½ atoms of magnesium in dry ether. The next morning one mole of acetopropanol diluted with two volumes of dry ether was added slowly. The reaction was not violent and a gray precipitate formed with each addition of ketol. The next morning the magma was poured onto ice, the ether separated and distilled. The remaining oil consisted largely of diisoamyl, showing that probably not more than 35% of actual isoamyl magnesium iodide was present in the system for each mole of isoamyl iodide added.

The crude glycol fraction, boiling about 150° at 15 mm was not large, not more than 50% of the theoretical on the acetopropanol used. This tertiary-primary glycol, as in the case of the other higher glycols, easily lost water upon distillation even at 15 mm. After distillation at 250 mm pressure, the oil was fractionated and gave a 40% yield of a fraction boiling at 107-109° under 12 mm pressure.

This fraction, dimethyl(3,7)octen(3)ol(1),* is a slightly yellowish oil with a sweet aromatic odor, somewhat resembling fine gum benzoin. It is soluble in the usual organic solvents and insoluble in water. It decolorizes a carbon tetrachloride solution of bromine and gives an acetate with acetic anhydrid.

Analysis. Calculated for $C_{10}H_{20}O$: C, 76.9%; H, 12.79%. Found: C, 76.1%; H, 12.44%.

VI. Preparation of higher lactones.

The mono-alkyl acetoacetic esters contain a hydrogen atom which is replaceable by organic radicles in the acetoacetic condensation. Isoamyl acetoacetic ester was prepared by boiling isoamyl iodide and sodium acetoacetic ester in absolute alcohol solution for some twenty-eight hours. The substituted ester had a boiling point 112-115° at 12 mm. (94).

Equimolar amounts of iodethyl acetate and sodium isoamyl acetoacetic ester were boiled in absolute alcohol solution for some twenty hours until a small portion added to phenolphthalein solution proved to be neutral. The excess alcohol was distilled off and the mother compounds removed as already described under acetobutanol. Yield 74%. The ester was not distilled because of its very high boiling point and danger of rearrangement.

This disubstituted acetoacetic ester is a reddish oil with a sweet odor. It is remarkable in that it is at one and the same time a primary alcohol, a ketone and a carboxylic acid. Thus it combines in one structure the three principal types of aliphatic compounds.

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*See note 2, p. 40.

Octonol(1)-carboxylic-acid(3) or Isoamyl-hydroxybutyric acid: The disubstituted acetoacetic ester, was hydrolysed with concentrated hydrochloric acid. Vigorous action took place and the flask was heated on the water bath for two hours. The oily layer was washed with water until the water showed only a faint turbidity with silver nitrate solution. The oil was then dried by standing in a desiccator for ten days over sulphuric acid. It was soluble in cold dilute sodium hydroxide solution but insoluble in water. Upon acidifying with hydrochloric acid the alkaline solution, the oil reappeared. With ethyl alcohol and sulphuric acid an ester with a fruity odor was formed. Yield about 60%.

Analysis. Calculated for $C_9H_{18}O_3$; H, 10.35%; C, 62.06%. Found: H, 10.39%; C, 61.95%C%**.

Nonyllactone or Isoamylbutyrolactone: The Oxynonylic acid was distilled under reduced pressure. It lost water at once and after two distillations boiled at 131-134° at 12 mm. pressure. It is a colorless sirupy oil with a pleasant peach-like odor. It is insoluble in cold dilute sodium hydroxide solution but dissolves upon boiling. It shows no reaction with acetic anhydrid and is resinified with concentrated sulphuric acid. Yield about 50% of the theoretical, calculated back to the iodoethyl acetate.

Analysis. Calculated for $C_9H_{16}O_2$: H, 10.27%; C, 69.27%. Found: H, 10.37%; C, 68.38%C%**.

Hydrolysis of disubstituted acetoacetic ester with dilute acid.

A small portion of the disubstituted ester was hydrolysed by boiling with 5% hydrochloric acid for eight hours. Carbon dioxide was given off vigorously at first. The water was extracted three times with ether, the ether removed and the residue distilled under a vacuum of 12 mm. Most of the product was an undistillable resin. The distillate was less than 10% of the ester taken. It was somewhat soluble in water and dissolved in bisulphite lye but no crystalline addition product could be obtained. Due to the small yield no combustion of the oil was run. Probably with weaker hydrochloric acid less resinification would be obtained.

Reaction between iodopropyl acetate and sodium acetoacetic ester: An equimolar mixture of iodopropyl acetate and the sodium salt of isoamyl acetoacetic ester in absolute alcohol solution was boiled for some twenty-two hours until neutral to phenolphthalein solution. The disubstituted ester, acetoxypropyl-isoamyl-acetoacetic ester, was obtained as previously described. It is a reddish oil with a very sweet characteristic odor, yield 71%.

The ester was hydrolysed by boiling with an excess of barium hydroxide. The precipitate of barium salt was acidified with hydrochloric acid. The oil so obtained was allowed to stand, because of illness, for some six weeks. It was then found to be insoluble in cold

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**See note 3, page 40.

dilute sodium hydroxide solution but it quickly dissolved upon warming.

Upon distillation in vacuo it did not distill until a temperature of over 180° at 15 mm. It possibly polymerized during its six weeks standing. However, the only decyllactone recorded in the literature (22) is stated to have a boiling point of 281° under ordinary pressure.

The figures obtained upon combustion would indicate that rearrangement had taken place, probably during the long standing of the oxyacid in the presence of a trace of hydrochloric acid. Without this interruption, the preparation of decyllactone would probably proceed as smoothly as that of nonyllactone.

NOTES.

1. The solvents used in determining solubility in the "usual organic solvents" were ethyl alcohol, ether and acetone.

2. The removal of water from the tertiary hydroxyl of the glycols prepared (pages 51-55) would give double bonds on either side of carbon atom carrying the hydroxyl group. As the position of the double bond was not determined, the alcohols formed from acetobutonol could have the double bond in either (4) or (5), and those from acetopropanol in either (3) or (4).

3. The analytical combustion of these olefine alcohols was very difficult, due to the explosive violence of the reaction of their vapors with oxygen. After trying many expedients, a short bent pyrex tube sealed at one end was found to be the best type of boat. A wide space between the boat and the cerium dioxide must be arranged. The temperature must be very carefully controlled. Two soda-lime bottles must be used.

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VITA.

Edward M. Slocum was born August seventh, 1882, in Knoxville, Tennessee. He was educated in the public schools of that city and at the University School. He was graduated from this school with honors in 1898. This same year he entered the sophomore class of the University of Tennessee. He was graduated from this university in 1901, as the Valedictorian of his class, while he was yet eighteen years of age.

He became a Chemist of the Chicago Chrome Works for two years. In 1903 he became one of the chemists of Armour and Company, being given charge of the chemical work of the Armour Oil and Lard Refinery. In 1904 he was made Chemist of the Armour Soap Works. A year later he was appointed Chief Chemist of the 31st Street Plant of Armour and Company.

In 1906 he took up a special study of the manufacture of synthetic perfume products, and then became manufacturing chemist for the Allen B. Wrisley Company of Chicago. Six years later he became Vice-President and Managing Director of the Wetlin Chemical Company in the manufacture of synthetic chemicals.

In 1914 he became Chief Chemist for the Far East of the United States Rubber System, in the standardization of the preparation of plantation rubber in the Far East. In 1917 he returned to the United States to take out a number of patents for the United States Rubber Company on the methods worked out in the East Indies. He returned to the Company's plantations in Sumatra that same year and remained there until the expiration of his contract in 1919.

He took up post graduate work then in Organic Chemistry at Columbia University. In 1920 he held one of the Dupont Fellowships in Chemistry. He has also been an Assistant in Chemistry of Columbia University, in Organic and Qualitative Chemistry.

He has been a consulting chemist for perfume and terpene products of the United States Customs Department at Chicago, and was an expert witness for the Government in the Pears Soap Case.

He is a member of Phi Lambda Upsilon Honorary Chemical Fraternity, and Sigma Xi Honorary Scientific Fraternity, and Phi Kappa Phi Honorary Fraternity.

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